prevent undesirable taste and discoloration. In the USSR, the recommended maximum permissible concentration of $KMnO_4$ is 0.1 mg/ℓ (as Mn). The recommendation is intended to prevent the discoloration of water by manganese (Shigan and Vitvitskaya, 1971).

For marine waters, the U.S. EPA (1976) has recommended a criterion for manganese of 0.1 mg/ℓ for the protection of consumers of marine mollusks. Although the rationale for this criterion is not detailed, it is partially based on the observation that manganese can bioaccumulate by "factors as high as 12,000" in marine mollusks.

9.2. SUMMARY OF TOXICITY

Manganese is an essential element for humans and animals. The concentration of manganese present in individual tissues, particularly in the blood, is controlled after ingestion by homeostatic mechanisms and remains remarkably constant in spite of rapid fluctuations in intake (Cotzias, 1958). The main routes of absorption are the gastrointestinal and respiratory tracts. Acute poisoning by manganese may occur in exceptional circumstances where large amounts of manganese compounds are ingested or inhaled. Freshly formed manganese oxide fumes of respirable particle size can cause metal fume fever but are not believed to cause permanent damage (Piscator, 1976). The most pronounced toxic effects of manganese are a CNS syndrome known as chronic manganese poisoning (manganism) and manganese pneumonitis.

The adverse effect on the CNS begins with a psychiatric disturbance followed by a neurologic phase resembling Parkinson's disease. Manganism has been well described in the literature with clinical details for case clusters (Flinn et al., 1940; Penalver, 1955; Rodier, 1955; Chandra et al., 1974). Cotzias (1962) described three phases -- a prodromal phase with insidious onset including psychiatric disturbances, the extrapyramidal

disease with symptoms of awkward speech and loss of skilled movement, and typical manganism with severe rigidity, tremor, and inappropriate emotional reactions.

Manganism has been reported in workers in ore crushing and packing mills, in the production of ferroalloys, in the use of manganese alloys in the steel industry and in the manufacture of dry cell batteries and welding rods. Very high concentrations of manganese have been found in mines where cases of manganism were reported. The manganese air concentration in the immediate vicinity of rock drilling in Moroccan mines was ~450 mg/m^3 in one mine and ~250 mg/m^3 in another (Rodier, 1955). In two reports from Chilean mines (Ansola et al., 1944a,b; Schuler et al., 1957) the air concentrations of manganese varied from 62.5-250 mg/m^3 and from 0.5-46 mg/m^3, respectively.

In ferromanganese factories, neurological and psychic disturbances indicating manganese poisoning have been observed at manganese levels as low as 2-5 mg/m^3 of air (Suzuki et al., 1973a,b).

While manganism and its association with manganese has been well described, a dose-response relationship in man cannot be evaluated because duration of exposure is not well documented. Also, early signs of the disease were sought in only a few studies (Saric et al., 1977; Tanaka and Lieben, 1969), and none of the reported studies employed a standard cohort design (e.g., there was no follow-up or comprehensive characterization of the exposed populations).

A high incidence of pneumonia and other respiratory ailments has been reported in workers with occupational exposure to manganese (Baader, 1937; Lloyd-Davies, 1946; Rodier, 1955; Saric, 1978) and in inhabitants living around factories manufacturing ferromanganese or manganese alloys (Elstad,

1939; Suzuki, 1970). The increased incidence of pulmonary disease found in exposure to low concentrations of manganese is not necessarily directly attributable to manganese itself. Manganese exposure may increase susceptibility to pneumonia or other acute respiratory diseases by disturbing the normal mechanism of lung clearance. Some investigators have suggested that long-term exposure to manganese may contribute to the development of chronic lung disease (Saric and Lucic-Palaic, 1977), but there is little data to demonstrate this conclusively, particularly at ambient levels.

Effects on the cardiovascular system include reports of decreased systolic blood pressure in humans occupationally exposed via inhalation (Saric and Hrustic, 1975). This symptom was also shown to occur experimentally in orally exposed rats (Kimura et al., 19. . Reports about the effects of manganese on human blood and hemoglobin show conflicting results that have not been resolved by animal studies. The studies are difficult to compare because of variations in exposure and in the severity of the effect.

There have been reports of impotence in a majority of workers affected by manganese (Chandra et al., 1974; Emara et al., 1971; Rodier, 1955; Penalver, 1955). There is some experimental evidence of reproductive effects in laboratory animals. Degenerative changes in the testes of rats have been produced by excessive levels of manganese administered by multiple intraperitoneal injections (Chandra, 1971; Singh et al., 1974, 1975; Chandra et al., 1975; Tandon et al., 1975; Shukla and Chandra, 1977) and by single intratracheal injections in rabbits (Chandra et al., 1973a). Chronic dietary exposure to manganese has caused decreased organ weight for the preputial gland, seminal vesicle and testis in mice (Gray and Laskey, 1980), and decreased serum testosterone levels and reduced pregnancy percentage in rats (Laskey et al., 1982).

Manganese dichloride increased the incidence of lymphosarcomas in DBA/1 mice following twice weekly subcutaneous or intraperitoneal injections for 6 months (DiPaolo, 1964), and elicited slightly elevated tumor incidence in a Strain A mouse lung tumor bioassay (Stoner et al., 1976). Single or repeated intramuscular injections of MnO_2 or manganese powder did not result in increased incidences of lymphosarcomas, leukemias or local sarcomas in either sex of F344 rats or female Swiss mice. However, repeated intramuscular injections of an organomanganese compound, MAA, elicited statistically significant increases in injection site tumors in both sexes of F344 rats (Furst, 1978). Oral administration of manganese powder for 12 months twice monthly did not induce lymphomas and/or leukemias or fibromas in either sex of F344 rats (Furst, 1978). Although the results of the studies with divalent manganese are suggestive of carcinogenic activity, non-natural routes of administration were employed.

Some reported animal studies imply a carcinogenic potential for manganese, but the data are inadequate to support this conclusion (i.e., local injection site sarcomas in F344 rats, a marginal response in Strain A mice, and inadequate data in the experiment with DBA/1 mice). No epidemiologic information relating manganese exposure to cancer occurrence in humans has been located. Using IARC criteria (IARC, 1980), the available evidence for manganese carcinogenicity would be rated inadequate for animals and "no data available" for humans (Group 3). Consequently, the documented toxic effects are of more practical concern.

9.3. SPECIAL GROUPS AT RISK

Several researchers have mentioned the marked differences in individual susceptibility to inhaled manganese (Rodier, 1955; Penalver, 1955; Cotzias,

1958). They speculated that this may have been caused by alcoholism, syphilis, carbon monoxide, lesions of the excretory system, or the physiological or pathological condition of the respiratory tract. While it is reasonable to assume that an individual with an impaired ability to clear inhaled manganese or to excrete absorbed manganese would be at increased risk of adverse effects, no studies exist to confirm this.

Experimental studies suggest that populations at greatest risk of adverse effects due to manganese exposure are the very young and those with iron deficiency. The evidence for increased absorption and retention of manganese occurring in iron deficiency was shown in an inhalation study in humans (Mena et al., 1969, 1974), dietary studies in humans (Thomson et al., 1971), and ingestion studies in experimental animals (Rehnberg et al., 1982; Kostial et al., 1980).

Ingestion studies give useful information on the effects of inhalation exposures because most inhaled manganese is cleared to the gastrointestinal tract. The early neonatal period may be critical for metal accumulation because the very young also have an increased intestinal absorption and retention of manganese. This has been demonstrated in preweanling mice and rats (Kostial et al., 1978; Rehnberg et al., 1980) and in infants (Mena et al., 1974). High retention of manganese in the tissues, particularly the liver and brain, is associated with the limited excretion of manganese in the preweanling rat (Miller et al., 1975).

Kostial et al. (1978) report that oral toxicity measured by LD_{50} values is greater in very young (2 weeks) as well as old (54 weeks) rats, but not as high as expected based on the rate of intestinal absorption. Although the neonate has not been shown to have increased sensitivity to metals, the early accumulation of manganese must be considered as an additional risk factor.

Another population at high risk is workers exposed to manganese at or near the recommended TLV. Because neurological symptoms have been reported at concentrations below this limit, the TLV of 5 mg/m^3 has a low margin of safety.

9.4. EFFECTS OF MAJOR CONCERN AND EXPOSURE/RESPONSE INFORMATION

9.4.1. Effects of Major Concern. The key health effects of manganese are in the CNS and the lungs. The effect on the CNS, manganism, is irreversible and severely incapacitating although not directly associated with lethality. The pulmonary effects reported at levels below 1 mg/m^3 are for the most part reversible but can limit function or impose disability such as increased wheezing, bronchitis, or increased susceptibility to respiratory illness. The lowest reported exposure levels associated with life threatening diseases such as pneumonia have been similar to ranges associated with chronic manganese poisoning, 0.3 and up for brain effects.

Several endpoints suggested as effects from exposure to manganese are nonspecific, inconclusive or lack documentation in humans, such as degenerative changes in the testes, or decreased blood pressure. Sexual dysfunction has often been reported as an early effect of manganism at levels associated with other effects on the CNS.

9.4.2. Exposure/Response Information. Tables 6-1 and 6-3 show that human exposure to levels below 5 mg/m^3 has been associated with adverse effects to the CNS. These effects are either advanced manganism or a constellation of signs indicative of early stages of the disease (Suzuki et al., 1973a; Chandra et al., 1981). There is some evidence suggesting that exposure to levels below 1 mg/m^3 is associated with nonspecific symptoms which are common in early manganism and with abnormal neurological findings. However, in studies at these levels the findings reported could not be definitively attributed to manganese exposure (Saric et al., 1977; Chandra et al., 1981).

Studies of respiratory effects in humans (summarized in Table 6-8) show pulmonary system adverse effects at levels below 1 mg/m^3. Schoolchildren exposed to manganese emissions estimated at ~3-11 $\mu g/m^3$ from a ferromanganese plant developed an increase in respiratory symptoms compared with controls such as sore throat, wheezing and sputum on arising (Nogawa et al., 1973). Saric and Lucic-Palaic (1977) reported increased chronic bronchitis in workers exposed to 0.4-16 mg/m^3 but the results at ambient levels <1 mg/m^3 (Saric et al., 1975) were inconclusive because no exposure-response relationship was seen and confounding factors were not controlled.

There are many pulmonary endpoints that vary according to level of exposure. Although exposure ranges are so broad that the exposure/response relationship is sometimes masked, a continuum of effects has been observed which qualitatively supports the pulmonary endpoint. Pulmonary effects reported and supported include pneumonia (Elstad, 1939; Lloyd-Davies, 1946; Wassermann and Mihail, 1961), chronic bronchitis (Lloyd-Davies, 1946; Saric and Lucic-Palaic, 1977), radiographic changes and fibrosis (Wassermann and Mihail, 1961) and airways disability (Nogawa et al., 1973).

Animal studies also qualitatively support the association between pulmonary effects and manganese exposure. Table 9-1 summarizes the animal studies of the adverse effects of manganese inhalation. Pathological changes and decreased resistance to infection occur in a variety of species at levels above 0.7 mg/m^3. Inflammatory reactions and decreased resistance to infection have been observed in mice (Malgetter et al., 1976; Adkins et al., 1980c). Nishiyama et al. (1975) report pulmonary congestion and inflammatory changes in mice and monkeys after 5 months exposure to 3 mg/m^3 and less severe changes at 0.7 mg/m^3. Suzuki et al. (1978) describe radiologic changes after 10 months of exposure to 3 and 0.7 mg/m^3.

TABLE 9-1

Studies of Manganese Inhalation in Animals -- Summary of Effect Levels

Species	Duration	Concentration (mg/m^3)	System Examined	Effects*	Reference
			MnO_2		
Mouse	14 days	0.7	pulmonary	pulmonary changes	Nishiyama et al., 1975
Monkey	5 months	0.7	pulmonary	pulmonary changes	Nishiyama et al., 1975
Monkey	10 months	0.7	pulmonary	inflammatory and radiographic changes	Suzuki et al., 19[illegible]
Mouse	14 days	3.0	pulmonary	reversible inflammatory changes	Nishiyama et al., 1975
Monkey	5 months	3.0	pulmonary	congestion	Nishiyama et al., 1975
Monkey	10 months	3.0	pulmonary	inflammatory and radiographic changes	Suzuki et al., 1978
Guinea pig	1 day	22	pulmonary	inflammatory reaction with bacterial challenge	Bergström, 1977
Mouse	1-4 days	109	pulmonary; mortality rate	increased mortality with bacterial challenge	Malgetter et al., 1976

TABLE 9-1 (cont.)

Species	Duration	Concentration (mg/m^3)	System Examined	Effects*	Reference
			Mn_3O_4		
Monkey	15 months	0.10	pulmonary neurologic	none observed	Coulston and Griffin, 1977
Rat, monkey	9 months	1.1	pulmonary neurologic	none observed	Ulrich, 1979c
Rat, monkey	9 months	0.11	pulmonary neurologic	none observed	Ulrich, 1979c
Rat	2 months	0.12 + engine exhaust	pulmonary	none observed	Moore et al., 1975
Hamster	2 months	0.12	pulmonary	none observed	Moore et al., 1975
Mouse	2 hours	0.89	pulmonary	none observed	Adkins et al., 1980a
Mouse	2 hours	0.22-2.66 + bacteria	mortality rate	increases in rate	Adkins et al., 1980c

*These results are described in greater detail in Chapter 6 and in Table 6-10.

Table 9-1 summarizes several studies which report no gross or microscopic changes after exposure to ~0.1 mg/m^3 Mn_3O_4.

Thus, the animal data qualitatively support a range of respiratory effects associated with exposure to manganese. Human data qualitatively describe such effects but have limited exposure/response information because exposure ranges are broad, cohorts are not followed for long time periods, and duration of exposure is unreported or variable within a study population.

The mechanisms for toxic effects other than carcinogenicity are consistent with the concept of a threshold. The conventional approach toward determining the threshold for noncarcinogenic toxicity is to bracket it by identifying the highest level at which no adverse effects are observed (NOEL) and the lowest level at which adverse effects are observed (LOAEL). Therefore, the health effects assessment for manganese, considering the data available, focuses on the highest NOELs in humans or on the LOAEL as available. These data can be supported by animal data by estimating human equivalent exposures from animal exposure/effect levels.

9.5. HEALTH HAZARD EVALUATION

9.5.1. Critical Effect and Effect Levels. The critical effect is that adverse health effect which occurs at the lowest level of exposure. In order to identify the critical effect, the highest no-observed-effect-level (NOEL) and the lowest-observed-adverse-effect-level (LOAEL) for relevant toxic effects are identified and compared. Qualitative results and dose/response data from experimental animals are compared with levels based on human experience. Studies in humans report effects on the respiratory symptoms at levels below 1 mg/m^3 whereas studies of effects on the CNS below this level are equivocal or negative. Two studies give exposure-response

information in humans for the critical effect. Nogawa et al. (1973) reported an increased prevalence of respiratory symptoms in schoolchildren exposed to [illegible] mg/m^3 manganese ambient from a ferromanganese plant. This is the LOEL for humans. Saric and Lucic-Palaic (1977) report an increased prevalence of chronic bronchitis in workers exposed to 0.4-16 mg/m^3; however, prevalence of chronic bronchitis in a group of workers exposed to 0.005-0.04 mg/m^3 did not differ from controls. These results do not contradict the results of Nogawa because 1) children may be expected to be more sensitive than male workers, and 2) the latter study had less statistical power because fewer subjects were involved.

NOELs could be derived from several studies reported in laboratory animals exposed to manganese oxides consisting largely of particles in the alveolar fraction (<2 μm, see Section 3.5.4.1.). These studies are summarized in Tables 6-10 and 9-1. Factors which compromise the use of these studied for NOELs are described below.

Coulston and Griffin (1977) did not perform tests of lung function, did not give details of the pathological examination and reported acariasis and associated pulmonary complications in a majority (8/12) of the animals studied. Moore et al. (1975) reported no gross or microscopic abnormalities; however, they observed the animals for only 8 hours/day and for only 56 days. Ulrich et al. (1979a,b,c) exposed rats and squirrel monkeys to three levels of manganese and a control for 9 months. Pulmonary function tests were performed only on the monkeys. This study also had deficiencies which reduced confidence in the range of negative findings reported. Due to the small group size of the monkeys (4 males and 4 females) and the large within group variability, it lacked sufficient statistical power to detect any but the largest changes in the parameters measured. The variability

could have been reduced by using more appropriate statistical analysis to control for within group variation. The description of lung pathology was inadequate. Negative results were reported at 1.15 mg/m^3; however, Suzuki et al. (1978) reported pathologic changes in the lungs of rhesus monkeys exposed to 700 $\mu g/m^3$ of MnO_2 for 10 months. Based on these data, the next highest NOEL reported by Ulrich et al. (1979a,b,c) was 0.113 mg/m^3. However, the repeated reports of the absence of gross and microscopic abnormalities at a similar level (0.1 mg/m^3) suggest that this level may be close to a threshold.

These data do not exclude the possibility that more subtle toxic effects on the lungs may occur at ~0.1 mg/m^3. Effects do occur at 0.7 mg/m^3. In order to compare the reported NOEL (0.1 mg/m^3) and the LOAEL (0.7 mg/m^3) to similar data in humans, it would be helpful to estimate a human intake equivalent to that of the experimental animals. The suggested approach is provided in the Appendix.

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APPENDIX

ESTIMATING HUMAN EQUIVALENT INTAKE LEVELS FROM ANIMAL STUDIES

TERMINOLOGY AND APPROACH

The quantitative evaluation of potential health hazards for noncarcinogenic toxicants is based upon estimates of the threshold exposure level for the critical effect. Exposure levels for each study are evaluated as follows:

NOEL — No-Observed-Effect Level: That exposure level at which there are no statistically significant increases in frequency or severity of effects between the exposed population and its appropriate control.

NOAEL — No-Observed-Adverse-Effect Level: That exposure level at which there are no statistically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control. Effects are produced at this level, but they are not considered to be adverse.

LOAEL — Lowest-Observed-Adverse-Effect Level: The lowest exposure level in a study or group of studies which produces statistically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

FEL — Frank-Effect Level: That exposure level which produces unmistakable adverse effects, ranging from reversible histopathological damage to irreversible functional impairment or mortality, at a statistically significant increase in frequency or severity between an exposed population and its appropriate control.

The threshold estimate is bracketed by the highest NOEL and the LOAEL. The values for the NOELs and LOAEL depend on which health effect is considered. The estimate of the human threshold level is more uncertain if based on data for animals rather than for humans since there is presently limited information on species differences regarding toxic responses. Nevertheless, given limited dose-response data for humans it is necessary to extrapolate from the animal data.

Human equivalent intake rate (HEI) is defined here as the exposure level estimated from animal data which would cause the same health effect in humans if continued over the same fraction of lifespan as used in the animal

study. The conversion for manganese assumes that if the ratio (exposure level)/(body surface area) is the same in humans as in the animal study, then effects of the same severity will occur.

CRITICAL EFFECTS AND ESTIMATED EFFECT LEVELS

The lowest exposure level for humans associated with adverse effects is an estimated LOAEL of 3-11 $\mu g/m^3$ (based on emissions from a ferromanganese plant) for respiratory effects in children reported by Nogawa et al. (1973). Comparison among studies of respiratory effects in laboratory animals (summarized in Table 9-1) shows that Ulrich et al. (1979a,b,c) and Suzuki et al. (1978) utilized the longest exposure periods at exposure concentrations ~100 $\mu g/m^3$. Although there are shortcomings in each study (see Section 9.5.) the repeated observations suggest that this level may be close to the threshold. Therefore, these studies were selected for these risk assessment calculations. The HEI is estimated from the data from experimental animals by the following:

$$HEI = C_A \times D_E \times Br \times \left(\frac{70\ kg}{W_a}\right)^{2/3}$$

where C_A = concentration in air in the animal study in $\mu g/day$

D_E = fraction of day experimental animals were exposed

Br = volume of air breathed per day in m^3

W_a = body weight of the experimental animal in kg

This conversion is based on the following assumptions:

1. Agents that are in the form of particulate matter are expected to be absorbed and retained proportional to the breathing rate.

2. The fraction retained is approximately the same for all species.

3. The conversion from animals to humans based on exposure level per body surface area more accurately reflects differences among species than does a mg/kg body weight conversion (Rall, 1969). The surface area ratio is well approximated by the body weight ratio to the 2/3 power (Calabrese, 1983).

The estimation of HEI is based on intake by inhalation of manganese in excess of dietary intake of this essential element because all studies used here were so designed. Also, a sufficient oral intake and strong homeostatic control can be assumed so that excess exposure is appropriate. Inhalation studies should be used since the critical effect is route specific.

The estimated HEI (in mg/day) is converted to a human equivalent exposure level (HEEL) by dividing by the average daily human respiratory rate of 20 m^3/day. All calculations are summarized in Table A-1.

In the studies considered here O_E equals 1. Therefore, for rhesus monkeys in the study by Suzuki et al. (1978)

$$HEI = C_A \times Br \times \left(\frac{70\ kg}{W_a}\right)^{2/3}$$

$$= 700\ \mu g/m^3 \times 1.4\ m^3/day \times \left(\frac{70\ kg}{3.5\ kg}\right)^{2/3}$$

$$= 7293\ \mu g/day.$$

The HEEL obtained by dividing by the daily respiratory volume (20 m^3/day) is 365 $\mu g/m^3$. Note that this HEEL is based on a LOAEL and thus may be above the human threshold level.

Similar calculations using data on rats from Ulrich et al. (1979a,b,c) (W_a = 0.35 kg, Br = 0.26 m^3/day, and C_A = 113 $\mu g/m^3$) result in a HEEL of 51 $\mu g/m^3$. For the Ulrich et al. (1979a,b,c) data on squirrel monkeys (W_a = 0.72 kg, Br = 0.72 m^3/day, and C_A = 113 $\mu g/m^3$) the HEEL is 87 $\mu g/m^3$.

These results, shown in Table A-1, can be compared with the data from Nogawa et al. (1973) on children who had an estimated LOAEL of 3-11 $\mu g/m^3$. The data obtained from human data is, of course, crucial for public health decision making. This level might be expected to be lower than the animal level for the following reasons: 1) the studies on animals

TABLE A-1

Exposure Effect Information for Health Hazard Evaluation: Human Equivalent Exposure Levels Estimated from Animal Data

Species	Response Level	Exposure ($\mu g/m^3$)	Animal Intake Level		Estimated Human Intake Level		Estimated Human Equivalent Exposure Level (HEEL) ($\mu g/m^3$)	Adjusted HEEL[a]	Reference
			µg/day	µg/kg/day	µg/day	µg/kg/day			
Rat	reported NOEL[b]	113	29	84	1022	15	51	5	Ulrich et al., 1979a,b,c
Squirrel monkey	reported NOEL[b]	113	81	113	1740	25	87	8.7	Ulrich et al., 1979a,b,c
Rhesus monkey	LOAEL	700	980	280	7293	104	365	36.5	Suzuki et al., 1978

[a]The estimated HEEL is adjusted by dividing by an uncertainty factor of 10 to compensate for the heterogeneity in human populations and thereby protect the sensitive individual.

[b]These NOELs are used to compare human and animal data despite some limitations which exist in the study. See text for further discussion.

have flaws resulting in uncertainty as to whether adverse effects are missed; 2) certain endpoints studied in humans cannot be ascertained as well in animal studies and are likely to be overlooked; and 3) children are a sensitive group. A better comparison between animal and human data is obtained by dividing the HEEL by 10 to compensate for the heterogeneity in the human population and to better protect the sensitive individual (Dourson and Stara, 1983). The range of adjusted HEELs from the animal NOELs and the LOAEL is 5-37 $\mu g/m^3$, and supports the human LOAEL of 3-11 $\mu g/m^3$ observed in a sensitive population.

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EXECUTIVE SUMMARY

The use of ceramic particulate traps, in conjunction with manganese fuel additives, has been viewed as a way to reduce emissions of particulate matter from diesel-fueled vehicles. This report focuses on the potential health effects from increased public exposure to manganese emissions from such a use.

Manganese is the 12th most abundant element on earth. Ambient levels of manganese rarely exceed 0.1 $\mu g/m^3$. Manganese is classified as an essential element for physiologic functions. Average daily intake of manganese, which is mostly from food, is about 3 to 4 mg/day (range 2 to 9 mg/day). Homeostatic mechanisms (primarily by regulation of intestinal absorption and biliary excretion) maintain the body burden of manganese between 12 and 20 mg.

The health effects of major concern from manganese exposure are neurotoxic and respiratory. Numerous studies, mostly in occupational groups exposed to very high levels of manganese (in the mg/m^3 range), have demonstrated that prolonged exposure to relatively high levels of manganese leads to manganism (a Parkinson-disease like syndrome) and other symptoms of central nervous system toxicity, as well as to pneumonitis, bronchitis, and increased susceptibility to pulmonary infections. Pulmonary effects of manganese have been observed to occur at lower levels of exposure than neurotoxic effects.

The health effects of exposure to low levels of manganese have not been well characterized. An epidemiologic

study (Saric et al. 1977) has reported neurotoxic effects of manganese at exposure levels that were between 300 and 5,000 $\mu g\ Mn/m^3$. Another epidemiologic study (Nogawa et al. 1973), which focused on respiratory symptoms in children attending a school near a ferromanganese plant, has reported health effects at levels as low as 3 to 11 $\mu g\ Mn/m^3$. However, serious problems with the study (such as poor characterization of exposure, failure to blind observers and to randomize students, and a lack of control for the confounding factors) suggest that the results of the study are not reliable. All other studies have reported adverse effects at levels that are one to two orders of magnitude greater.

A modeling study by Volkswagen (1984) for emissions of manganese suggests that the worst-case ambient concentration of manganese in an urban street canyon is likely to be less than 0.5 $\mu g/m^3$ (the assumptions include 6.6 percent penetration of the manganese technology into the vehicle fleet, emissions of 100 percent of the manganese added to the fuel in the emissions, high manganese consumption, and worst-case traffic conditions). HEI has independently verified the Volkswagen calculations. If an individual, such as a traffic policeman, worked outdoors all day in a street with the worst-case levels of manganese, his daily intake of manganese by inhalation from ambient sources would be 3.6 μg. This is a very small amount compared to the daily dietary intake of manganese (3 to 4 mg/day), and is not expected to tax the body's homeostatic mechanisms that regulate manganese.

On the basis of the information in the literature, and the exposure and dose of manganese estimated in this report and summarized above, it appears very unlikely that exposure to airborne manganese from mobile sources (worst-case level 0.5 $\mu g/m^3$) would produce adverse neurologic effects.

Regarding respiratory effects, the difference between estimated exposure (worst-case level 0.5 μg Mn/m^3) and the lowest level at which health effects have been reported in the Nogawa et al. (1973) study (3 to 11 μg Mn/m^3) is not very large. However, in view of the concerns regarding the Nogawa study, it appears unlikely that the increased ambient levels of manganese from trap-equipped diesel vehicles would produce adverse respiratory effects.

Given the paucity of information at the anticipated low levels of manganese from its use in diesel-powered vehicles, if manganese were to be used as a fuel additive, it is very important that the emissions of manganese be characterized in terms of their physical form and chemical species, the assumptions made in estimating the emissions, exposure, and dose of manganese be substantiated, and the results of the Nogawa study be reviewed and evaluated in greater depth than attempted in this report.

INTRODUCTION

Combustion of diesel fuel results in the formation of fine carbonaceous particles, a number of organic compounds that can adsorb to the particles, and a number of gases. Because of concerns with the health effects of diesel emissions, the U.S. Environmental Protection Agency (EPA) has promulgated regulations that are aimed at reducing the emission of particulate matter from diesel-powered vehicles. The EPA has also mandated that the emissions of nitrogen oxides from diesel-powered automobiles be reduced. However, because of the nature of the combustion process, technologies for reducing particulate emissions tend to increase emissions of oxides of nitrogen, and vice versa. The general approach adopted in the automobile industry to meet these regulations